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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 04/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/797,946	WILEY ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-25 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-25 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 6/17/04;11/26/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims:

Claims 1-25 are pending.

Claims 1-25 are rejected.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on June 17, 2004 and November 26, 2004 has been acknowledged.

Claim Rejections - 35 USC § 112-2

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 4, 6, 8, 12, 13, 15, 17, 18, 21, 22, 24, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 12 are indefinite. What is meant by the phrase and/or? Is the phrase and/or referring to preventing or a condition associated with calcium? Does the phrase refer to preventing and treating in the alternative or the conjuction?

Claims 1 and 12 also contains the word safe, what is meant by safe, or rather what is safe versus effective.

The term "from about" in claims 2, 4, 6, 8, 12, 13, 15, 17, 18, 21, 22 and 24 is a relative term which renders the claim indefinite. The term "from about" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite

degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Because one of skill will not be able to determine which term is in control.

Claims 6 and 8 are also unclear to the phraseology "on an elemental calcium basis). What does this mean and is it necessary for the claim?

The following is a quotation of the first paragraph of 35 U.S.C. 112:1

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for decreasing serum level of triglycerides in mammals, does not reasonably provide enablement for preventing condition associated with calcium and or magnesium deficiency. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

For rejections under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400, 1404 (CAFC, 1988)):

1) Nature of invention.

2) State of prior art.

3) Quantity of experimentation needed to make or use the invention based on the content of the disclosure

4) Level of predictability in the art.

5) Amount of direction and guidance provided by the inventor.

6) Existence of working examples.

7) Breadth of claims.

8) Level of ordinary skill in the art.

See below:

In the instant case, applicants are claiming in part, a method of preventing a condition associated with calcium and or magnesium deficiency in a human and in part, treating, to alleviate the pathological effects of any and all calcium or magnesium deficiency (claim 1), administering a pharmaceutical formulation containing a therapeutically effective amount of the compound calcium 3-hydroxy-3-methylbutyrate or magnesium 3-hydroxy-3-methylbutyrate useful for the treatment and/or amelioration of osteoporosis, hypertension and bone loss (claim 10).

1) Nature of the invention.

The nature of the invention is directed to methods of treating/preventing in a human to alleviate the pathological effects of calcium or magnesium deficiency, comprising administering the instant compound to a patient (human) in need thereof. As stated, however, claim 1 includes within its scope, any calcium or magnesium deficiency condition or disease.

A. Treatment by condition associated with calcium type

There is no one particular antibone loss agent that is effective for all forms of osteoporosis. There is no one treatment, or combination of treatments which provides prevention (not occurring even the first time) of fractures due to osteoporosis. The best

prevention, however, is a life-long commitment to physical activity, good nutrition, and normal reproductive hormone status. (See www.endocrineweb.com/osteoporosis/treatment.htmlWeb), however, this is not prevention , all of which help reduce osteoporosis but do not prevent.

As discussed below, (see http://www.endocrineweb.com/osteoporosis/treatment.html), teaches that researchers face the problem of sifting through potential conditional drugs with Ca or Mg to find ones promising enough to make. Treatment of osteoporosis is classified in two groups and non of the drugs have proven themselves yet (see www.endocrineweb.com/osteoporosis/treatment.html). While the state of the art is relatively high with regard to the treatment of osteoporosis with specific agents, for a compound or genus to be effective against condition associated with calcium or magnesium generally is contrary to medical science. Thus a considerable amount of invivo and invitro testing is required before the agent can be considered for a particular type of disease.

B. Chemotherapy

www.endocrineweb.com/osteoporosis/treatment.html teaches that There is no one treatment, or combination of treatments which provides prevention (not occurring even the first time) of fractures due to osteoporosis. At the present time, only anti-resorbers are approved in the United States by the FDA for use in treating osteoporosis and none of the drugs in this group have demonstrated prevention.

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher,* 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. Further, their mode of action is often unknown or very unpredictable and administration of the drugs can be accompanied by undesirable side effects.

2) State of the prior art and the predictability or lack thereof in the art.

The state of the prior art is that it involves a myriad of diseases such as sleep disorder, ovulation, fibromalgia bone loss behavioral problem etc thus preventing or treating will include screening *in vitro* and *in vivo* to determine the effect of the compound on the specific disease. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. The instant claimed invention is highly unpredictable as discussed below:

Thus, in the absence of a showing of correlation between all the conditions associated with calcium or magnesium deficiency claimed as capable of being treated by compounds of the instant claims, one of ordinary skill in the art is unable to fully predict possible results from the administration of the compounds due to the unpredictability of the role of bone fracture for example.

3) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The quantity of experimentation needed is undue experimentation. One of ordinary skill in the art would first need to determine the type of conditions associated with calcium or magnesium, and then determine which of the thousands of compounds would be suitable for said treatment and/or prevention. Note that osteoporosis is only one such condition. There are others, e.g., diabetic, renal disease, encephalopathy for which the current specification provides no guidiance.

4) Level of predictability in the art.

The art pertaining to the treatment of all calcium and magnesium conditions remain highly unpredictable. As disclosed above, there is no absolute predictability even in view of the seemingly high level of skill in the art. Firstly, for a compound or genus to be effective against oesteoporosis for example or a disease associated with calcium conditions/magnesium generally is contrary to medical science. Conditions associated with calcium is a process that can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the conditions associated with calcium reaction. Accordingly, treatments for conditions associated with calcium are normally tailored to the particular type of of mediator present, as there is no, and there can be no "magic bullet" against all conditions associated with calcium related diseases generally.

5) Amount of direction and guidance provided by the inventor.

The amount of direction or guidance present is nowhere found in the specification. However, the gap between the teaching in the specification of *in vitro* activity and *in vivo* is large enough to warrant thorough and compelling *in vivo* data

especially in the absence of working examples demonstrating the full scope of all calcium and magnesium related diseases and conditions.

6) Existence of working examples.

As discussed above, no working example is found. Applicant's omission of working examples does not enable one of ordinary skill in the art to treat the numerous amounts of diseases encompassed by the instant invention.

7) Breadth of claims.

Claim 1 is extremely broad due to the vast number of possible diseases encompassed by the instant invention. Condition associated with calcium and or magnesium involves a myriad of diseases such as sleep disorder, ovulation, fibromalgia bone loss behavioral problem etc.

8) Level of ordinary skill in the art.

Due to the unpredictability in the pharmaceutical art (see referencewww.endocrineweb.com/osteoporosis/treatment.htmlWeb), it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Hence, the specification fails to provide sufficient support of the broad use of the compounds of the claims for the treatment of any disease. As a result necessitating one of ordinary skill in the art to perform an exhaustive search to determine which diseases can be treated by what compounds of the instant claims in order to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 1, 3, 5-6, 9, 11-12 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Nissen et al. US 6,031,000.

Nissen et al disclose the current claims 1, 3, 6, 12 and 14 administering calcium 3-hydroxy-3-methylbutyrate (ca-HMB)(see col. 3 lines 62+) to increase the aerobic capacity of muscle of an animal, administering a dose (effective amount- see col. 3 lines 60+) of ca-HMB. Calcium is also involved in a wide variety of other functions, including blood coagulation, the transmission of nerve impulses, muscle contraction and relaxation, normal heartbeat, stimulation of hormone secretion and the activation of enzyme reactions. Consequently, the reference anticipates the claimed invention defined in claims 1 and 5.

With regard to claim 3, the pharmaceutically carrier is (see col. 3 lines 55+), administering 10 g an equivalent to 1000 mg of ca-HMB (see col. 3 lines 65+) as in claim 6 in a solid dosage form recited in claim 9 (see col. 3 lines 55+) wherein the form is of a food product (see col. 6 lines 55+) as in the current claim 11.

II. Claims 1, 5-6 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Vukovich et al. American Soc. Nutr. Sci.

Vukovich et al disclose the current claim 1and 5 administeration of an effective amount of calcium 3-hydroxy-3-methylbutyrate to treatloss of muscle mass (see page 2049) i.e., a condition associated with calcium deficiency as disclosed in the current claim 1. Consequently, the reference anticipates the claimed invention defined in claim 1.

As to claim 6 the reference discloses administering calcium 3-hydroxy-3-methylbutyrate at 250 mg (see page 2049 under study design) in a solid form-capsule as in current claim 9.

III. Claims 1, 5-6, 7-9, 12 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 94/17678.

WO 94/17678 discloses the instant claims 1 and 12 administering 3-hydroxyl -3-methylbutyrate (see page 7), wherein the mineral supplement is calcium 3-hydroxyl -3-methylbutyrate as in claim 5 (at page 9) by administering at a level of 1000 mg (see page 9) as in claim 6. The reference also teaches various salts forms of the 3-hydroxyl -3-methylbutyrate, magnesium can be employed, therefore it will be obvious the teachings of claims 7 and 8.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nissen et al. US 6,031,000 taken with Vukovich et al. American Soc. Nutr. Sci. and WO 94/17678 in view of www.naturalconnections.com (1998).

Nissen et al teach the current claims 1, 3 and 6 administering calcium 3-hydroxy-3-methylbutyrate (ca-HMB)(see col. 3 lines 62+) increasing the aerobic capacity of muscle of an animal, administering a dose (effective amount- see col. 3 lines 60+) of ca-HMB. calcium is also involved in a wide variety of other functions, including blood coagulation, the transmission of nerve impulses, muscle contraction and relaxation, normal heartbeat, stimulation of hormone secretion and the activation of enzyme reactions.

With regard to claims 3, 14 and 22 having a pharmaceutically acceptable carrier starch (see col. 3 lines 55+), administering 10 g an equivalent to 1000 mg of ca-HMB (see col. 3 lines 65+) as in claims 6 in a solid dosage form recited in claims 9 and 20

(see col. 3 lines 55+) wherein the form is of a food product (see col. 6 lines 55+) as in the current claims 11 and 25.

As to claim 19 Nissen teaches the edible form of 3-hydroxy-3-methylbutyrate dissolved in a liquid (a bioavailable and water soluble) (see col. 6 line 55+)

Vukovich et al teach the current claim 1and 5 administering an effective amount of calcium 3-hydroxy-3-methylbutyrate (see page 2049 under study design) treating loss of muscle mass (see page 2049) (thus any condition associated with calcium deficiency) as taught in the current claim 1.

As to claim 6 the Vukovich reference discloses administering calcium 3-hydroxy-3-methylbutyrate at 250 mg (see page 2049 under study design) in a solid form-capsule as in current claim 9.

WO 94/17678 teaches teach the instant claims 1 and 12 administering 3-hydroxyl -3-methylbutyrate (see page 7), wherein the mineral supplement is calcium 3-hydroxyl -3-methylbutyrate as in claim 5 (at page 9) by administering at a level of 1000 mg (see page 9) as in claim 6. The reference also teaches various salts forms of the 3-hydroxyl -3-methylbutyrate, for example calcium, magnesium and potassium. Therefore it would have been obvious to use the salts of magnessuin as claimed in claims 7 and 8.

Naturalconnections.com teaches the current claim 2, 13 and 21 limitation (s) of the ratio of calcium to magnesium is 2:1(see enclosed reference). The reference also teaches administering the supplemental amount of calcium and magnesium for bone health.

Although, the above cited references did not per-se teach the current claims 4, 15 and 23 wherein the concentration of the pharmaceutically acceptable carrier is 0.1% would have been obvious to one of ordinary skill in the art as pharmaceutical carriers are well known in the pharmaceutical field and the concentration of the carrier would depend on the amount of active ingredient present (see Nissen et al, col. 3 lines 58-60).

Next, the method differs in current claims 17-19 wherein the concentration of the unit dosage is from 730 mg to 7,300 mg of calcium (1-10) and 200 mg to 2,000 mg magnesium (1-10). The amount of calcium content as taught by www.naturalconnections.com is 750 mg twice as much as the amount of magnesium present in the supplement. Based on that the determination of a dosage having the optimum therapeutic index is well within the level of the ordinary skill in the art, and the artisan would be motivated to determine the optimum amounts to get the maximum effect of the drug, hence the reference makes obvious the instant invention.

Even though the reference did not directly teach the condition osteoporosis or bone loss, it is well known in the art that calcium and magnesium supplements are used for maintaining the bone structure, advertised daily to drink milk which contains high calcium content. One of ordinary skill in the art would have been motivated to use the combination of 3-hydroxy-3-methylbutyrate salts (Ca-Mg) to promote healthy bones.

Thus, the claimed invention was prima facia obvious to make and use at the time it was made.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or

discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-25 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-25 of copending Application No. 10/658075. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. The claims are word for word identical with that of the co-pending application 10/658075.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SVG
4/7/06

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